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EXAMINER	
LI, BAO Q	

ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/524,549	LUSSO ET AL.	
	Examiner	Art Unit	
	BAO LI	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *1-22, 29-31* is/are withdrawn from consideration.

5)☒ Claim(s) *26* is/are allowed.

6)☒ Claim(s) *23-25,27 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 April 2008* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

The response and amendment filed on April 02, 2008 has been acknowledged. Claims 23 and 26 have been amended. Claims 1-31 are pending. Claims 1-22 and 29-31 were withdrawn from consideration. Claims 24-28 are considered before the examiner.

Declaration

The Declaration filed under 37 C.F.R. 1.132 by Dr. Samuele Burastero has been acknowledged.

Specification

1. The specification has been amended to including the hybridoma deposit information and assurances statement, which effectively overcome the deposit issue.

Withdrawn Claim Rejections - 35 USC § 101

2. The rejection of claim 23 under 35 U.S.C. 101 as being directed to non-statutory subject matter has been moot in view of a new ground rejection necessitated by Applicants' amendment.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. The rejection of claims 24-25 are still rejected under 35 U.S.C. 112, first paragraph because the specification does not provide sufficient evident to support that the isolated antibody binding to the HIV-1 envelope is able to prevent HIV-1 infection or a disease or condition related to the immune system of the subject.

5. Applicants traverse the rejection and provide a declaration under 37 C.F.R. 1.132 by Dr. Samuele Burastero filed on April 14, 2008 (Appendix A) as further support for enablement disclosure. Applicants assert that the Burastero declaration includes data on DB-81 antibody; the

affinity of DB-81 for the CD4/env complex, DB-81 antibody can block different HIV-1 envelope mediated fusions in target cells expressing both CCR5 and CXCR4.

6. Applicants' argument and Declaration have been respectfully considered; however, it is still not persuasive. Because although the isolated antibody can block both M-tropic and T-tropic HIV-1 envelope proteins mediated fusions, it cannot prevent the HIV-1 infection.

7. Applicants thus believe that a person having ordinary skill in the art how to use the invention commensurate in scope with the claims. Applicants respectfully request reconsideration and withdraw this rejection with respect to claims 24 and 25.

8. Applicants' argument has been fully considered; however, it is not found persuasive. Because although the claimed monoclonal antibody DB-81 can recognize both T cell tropic and monocyte-tropic HIV-1 envelopes and block the envelope mediated fusions as Applicants asserted in the response, the scope of the claims read on using any antibody to prevent the HIV infection, as long as said antibody recognizes any HIV envelope protein gp120 that forms a complex with sCD4.

9. Applicants' argument has been respectfully considered; however, it is not persuasive. Because the specification does not provide sufficient evidence to support that blocking the HIV-1 envelope/CD4 mediated fusion can prevent the HIV-1 infection since the broad scope of the claims read using said antibody to prevent HIV-1 infection. It is well known in the art that a direct administration of a neutralizing antibody against HIV-1 envelope can block a virus infection via blocking the HIV-1 envelope protein mediated fusion. However, this is only a passive immunization, and it can never induce any active immunization leading to prevent the HIV infection in the future. A person ordinarily skilled in the art would not accept that any antibody administration is able to induce a preventive immunity against HIV-1 infection either. Therefore, the rejection of the claims is maintained.

10. The rejection of claims 23-28 under 35 U.S.C. 112, first paragraph has been removed because Applicants provide the deposit number and deposit information related to the claimed hybridoma cell line CBA ICLB.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 23-24 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Kang et al. (J. Virol. 1996, Vol. 68, No. 9, pp. 5854-5862).

13. Applicants traverse the rejection and submit that claim 23 relates to an isolated antibody immunospecific for a fixed cell expressing an HIV envelope encoded by the gene of gp 160, wherein the envelope is further complexed with a CD4 receptor. Claim 26 relates to a hybridoma cell line having the identifying characteristics of the cell line deposited with the Advanced Biotechnology Center Inter Lab Cell Line Collection (CBA ICLB) under Deposit number PD03002 wherein the hybridoma produces DB-81. However, 1). Kang describes antibodies produced by immunizing animals with soluble CD4/gp120 complex (i.e. conjugates with monomeric HIV envelope protein gp 120); the antibody is not immunospecific for a fixed cell that includes an HIV envelope complex encoded by gp 160 and further wherein the envelope is complexed with a CD4 receptor; 2). Kang also does not describe a hybridoma cell line under Deposit number PD03002 wherein the hybridoma produces DB-81. Since claims 24 and 28 depend from claims 23 and 26 respectively, claims 24 and 28 are not anticipated by Kang.

14. Applicants' argument has been fully considered; however, it is not found persuasive for the following reasons:

15. 1). The antibody described by Kang et al. is same to the claimed antibody that can recognize HIV-1 gp120 or the HIV-1 gp120 expressing on the cell surface inherently. Since it is produced by immunization of mice with gp120/CD4 complex.

16. While the claimed is now amended to an antibody immunospecific for cell comprising an HIV envelope complex encoded bybgp160 and further wherein the envelope binds to CD4, the envelope protein actually bound by the antibody could still be gp120 or usually is gp120. Because it is well known in the art that the gp160 is the precursor of HIV-1 envelope encoded by the full length of HIV-1 envelope protein. When it is expressed as precursor, it is remained in the

intracellular portion, then it is cleaved into the membrane bound portion of envelope, i.e. gp120 and trans membrane domain of HIV-1 envelope of gp41. The method taught by specification **in example 2 on page 41** describe to immunize mice with cell expressing complex of gp120 and sCD4 on the cell surface. The gene used for transforming the cell can be either gene encoding the HIV-1 gp120 or the full length of HIV-1 envelope protein gene of gp160. However, upon the gene of gp160 is expressed in a eukaryotic cell, it is inherently cleaved into envelope protein gp120 and gp41 as the final product, unless the cell is deficient in such proteinase cleavage, wherein the CD4 binding site is located on the gp120. In the instant case, the specification does not teach that the cell can expressed uncleaved gp160 binding to CD4. It only teaches that the HIV-1 gp120 is expressed, which binds CD4 as a complex. The complex expressed by the cell is used as an antigen to induce the antibody. To this context, the antibody disclosed by Kang is same as the claimed antibody.

17. 3). The antibody cited in claim 28 is directed to a genus of antibodies that bind to the same idiotype of antibody produced by the hybridoma of claim 26. Therefore, it may include the antibody cited in claim 26, but it is not limited to the antibody of claim 26. Claim 28 is broader scope than claim 26. It does not depend on claim 26. Therefore, the antibody disclosed by Kang et al. still meets the limitation of claim 28.

18. 4). Claim 26 is directed to a specific isolated antibody with deposit number. But it is not rejected.

19. Therefore, the antibody described by Kang et al. inherently meet the limitation of the claimed antibody. The rejection is therefore, maintained.

20. Claims 23-24 and 28 are still rejected under 35 U.S.C. 102(b) as being anticipated by Devico et al. (Virol. 1996, Vol. 218, pp. 258-263).

21. Applicants argue that 1). Devico et al. teach a method of making the antibody via immunizing the mice with cross-linked gp120 with CD4 complex, the antibody is not immunospecific for a fixed cell expressing HIV envelope complex encoded by gp 160, wherein the envelope is complexed with a CD4 receptor; and 2). Devico et al. also does not describe a hybridoma cell line under Deposit number PD03002, wherein the hybridoma produces DB-81.

Since claims 24 and 28 depend from claims 23 and 26 respectively, claims 24 and 28 are not anticipated by Devico et al.

22. Applicants' argument has been fully considered; however, it is not found persuasive for the following reasons:

23. 1). Devico et al. provide a method of producing an anti-HIV –1 antibody by immunizing the mice with a soluble CD4-gp120 complex, wherein said antibody can inhibit several glades of HIV infection (See Figs. 1-2 and Abstract). Therefore, the antibody is the same antibody to the claimed antibody because it is induce by the immune complex of gp120/CD4, it inherently recognize the gp120/CD4 complex.

24. 2). While the claimed is now amended to an antibody immunospecific for cell comprising an HIV envelope complex encoded bybgp160 and further wherein the envelope binds to CD4, the envelope protein actually bound by the antibody could still be gp120 or usually is gp120. Because it is well known in the art that the gp160 is the precursor of HIV-1 envelope encoded by the full length of HIV-1 envelope. When it is expressed as precursor, it is t remained in the intracellular portion, then it soon be cleaved into the membrane bound portion of envelope, i.e. gp120 and trans membrane domain of HIV-1 envelope of gp41. The method taught by specification **in example 2 on page 41** describe to immunize mice with cell expressing complex of gp120 and sCD4 on the cell surface. The gene used for transforming the cell can be either gene encoding the HIV-1 gp120 or the full length of HIV-1 envelope protein gene of gp160. However, upon the gene of gp160 is expressed in a eukaryotic cell, it is inherently cleaved into envelope protein gp120 and gp41 as the final product, unless the cell is deficient in such proteinase cleavage, wherein the CD4 binding site is located on the gp120. In the instant case, the specification does not teach that the cell can expressed uncleaved gp160 binding to CD4. It only teaches that the HIV-1 gp120 is expressed, which binds CD4 as a complex. The complex expressed by the cell is used as an antigen to induce the antibody. To this context, the antibody disclosed by Devico et al. is same as the claimed antibody.

25. 3). The antibody cited in claim 28 is directed to a genus of antibodies that bind to the same idiotype as antibody produced by the hybridoma of claim 26. To this context, it may include the antibody cited in claim 26, but it is not limited to the antibody cited in claim 26.

Claim 28 is broader than claim 26. It does not depend on claim 26. Therefore, the antibody disclosed by Devico et al. still meets the limitation of claim 28.

26. 4). Claim 26 is not rejected, while applicants argue that claim 26 is directed to an antibody with particular deposit number.

27. As discussed above, the antibody taught by Devico et al. inherently possess the characteristic cited in claims 23-24 and 28, the rejection is therefore, maintained.

28.

29. Claims 23-24and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Celada et al. (J. Exp. Med. 1990, Vol. 172, pp. 1143-1150).

30. Applicants did not file any response to this rejection; the rejection is therefore, maintained.

31. Claims 23-24 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Konopka et al. (J. Gene. 1995, Vol. 76, pp. 669-679).

32. Applicants admit that Konopka describes a monoclonal antibody "raised in mice immunized with soluble CD4- gpl20 complex", Applicants still assert that 1). Konopka et al. do not describe an isolated or synthesized antibody immunospecific for a fixed cell that includes an HIV envelope complex encoded by gp 160 and further wherein the envelope is complexed with a CD4 receptor; 2). Konopka et al. also do not describe a hybridoma cell line under Deposit number PD03002, which produces DB-81. Since claims 24 and 28 depend from claims 23 and 26 respectively, claims 24 and 28 are not anticipated by Konopka et al. for at least the reasons described above. Applicant respectfully requests reconsideration and withdrawal of this rejection.

33. Applicants' argument has been fully considered; however, it is not found persuasive for the following reasons:

34. 1). Konopka et al. provide a monoclonal antibody, Mab F-91-55) raised against complex of soluble CD4 and HIV-1 gp120, wherein said antibody can inhibit synsytium formation and chronically infection of HIV-1 to the target cell. It meets all limitation required by the antibody cited in the rejected claims. Therefore, the antibody taught by Konopka et al. meet limitation of antibody cited in the claims.

35. 2). While the claimed is now amended to an antibody immunospecific for cell comprising an HIV envelope complex encoded bybgp160 and further wherein the envelope binds to CD4, the envelope protein actually bound by the antibody could still be gp120 or usually is gp120. Because it is well known in the art that the gp160 is the precursor of HIV-1 envelope encoded by the full length of HIV-1 envelope protein gp160. When it is expressed as precursor, it is remained in the intracellular portion, then it soon be cleaved into the membrane bound portion of envelope, i.e. gp120 and trans membrane domain of HIV-1 envelope of gp41. The method taught by specification **in example 2 on page 41** describe to immunize mice with cell expressing complex of gp120 and sCD4 on the cell surface. The gene used for transforming the cell can be either gene encoding the HIV-1 gp120 or the full length of HIV-1 envelope protein gene of gp160. However, upon the gene of gp160 is expressed in a eukaryotic cell, it is inherently cleaved into envelope protein gp120 and gp41 as the final product, unless the cell is deficient in such proteinase cleavage, wherein the CD4 binding site is located on the gp120. In the instant case, the specification does not teach that the cell can expressed uncleaved gp160 binding to CD4. It only teaches that the HIV-1 gp120 is expressed, which binds CD4 as a complex. The complex expressed by the cell is used as an antigen to induce the antibody. To this context, the antibody disclosed by Konokpa et al. is same as the claimed antibody.

36. 3). The antibody cited in claim 28 is directed to a genus of antibodies that bind to the same idiotype of antibody produced by the hybridoma of claim 26. Therefore, it may include the antibody cited in claim 26, but it is not limited to the antibody of claim 26. Claim 28 is broader scope than claim 26. It does not depend on claim 26. Therefore, the antibody disclosed by Konopka et al. still meets the limitation of claim 28.

37. 4). Claim 26 is directed to a specific isolated antibody with deposit number. But it is not rejected.

38. Therefore, the antibody described by Konopka et al. inherently meet the limitation of the claimed antibody. The rejection is therefore, maintained.

39.

40. Claims 23-24 and 28 are still rejected under 35 U.S.C. 102(b) as being anticipated by Sullivan et al. (J Virol. 1998 June; 72(6): 4694–4703).

41. In the response, Applicants provide the same arguments as listed above to traverse the rejection asserting that the method of making the antibody by Sullivan et al. is different from the claimed method. Furthermore, Sullivan et al. do not describe an isolated or synthesized antibody immunospecific for a fixed cell that includes an HIV envelope complex encoded by gp 160 and further wherein the envelope is complexed with a CD4 receptor. Sullivan et al. also do not describe a hybridoma cell line under Deposit number PD03002, which produces monoclonal antibody DB-81. Since claims 24 and 28 depend from claims 23 and 26 respectively, claims 24 and 28 are not anticipated by Sullivan et al. for at least the reasons described above. Applicant respectfully requests reconsideration and withdrawal of this rejection.

42. Applicants' argument has been fully considered; however, it is not found persuasive for the following reasons as discussed above:

43. 1). Sullivan et al. teach the antibody, which is same as the claimed antibody that can recognize the gp120/CD4 complex induced at the CD4 presence. While Sullivan et al. teach using EB virus transformed peripheral blood B cell, the immunization id still using the gp120/CD40 complex, the two monoclonal antibodies produced by said method, 17b and CG10 can recognize soluble CD4-inducible gp120 epitopes in the glycoprotein complex. The 17b antibody has been shown to neutralize HIV-1, especially in the presence of sCD4. The CG10 antibody can bind and neutralize the functional HIV-1 envelope glycoprotein complex in the presence of sCD4 and neutralizes the virus with the HXBc2 envelope glycoproteins (See entire document, especially Figs 1, 4, 5, 7). Therefore, the claimed invention is anticipated by the cited reference.

44. 2). While the claimed is now amended to an antibody immunospecific for cell comprising an HIV envelope complex encoded bybgp160 and further wherein the envelope binds to CD4, the envelope protein actually bound by the antibody could still be gp120 or usually is gp120. Because it is well known in the art that the gp160 is the precursor of HIV-1 envelope encoded by the full length of HIV-1 envelope glycoprotein gp160. When it is expressed as precursor, it is remained in the intracellular portion, then it soon be cleaved into the membrane bound portion of envelope, i.e. gp120 and trans membrane domain of HIV-1 envelope of gp41. The method taught by specification **in example 2 on page 41** describe to immunize mice with cell expressing complex of gp120 and sCD4 on the cell surface. The gene used for transforming the cell can be

either gene encoding the HIV-1 gp120 or the full length of HIV-1 envelope protein gene of gp160. However, upon the gene of gp160 is expressed in a eukaryotic cell, it is inherently cleaved into envelope protein gp120 and gp41 as the final product, unless the cell is deficient in such proteinase cleavage, wherein the CD4 binding site is located on the gp120. In the instant case, the specification does not teach that the cell can expressed uncleaved gp160 binding to CD4. It only teaches that the HIV-1 gp120 is expressed, which binds CD4 as a complex. The complex expressed by the cell is used as an antigen to induce the antibody. To this context, the antibody disclosed by Sullivan et al. is same as the claimed antibody.

45. 3). The antibody cited in claim 28 is directed to a genus of antibodies that bind to the same idiotype of antibody produced by the hybridoma of claim 26. Therefore, it may include the antibody cited in claim 26, but it is not limited to the antibody of claim 26. Claim 28 is broader scope than claim 26. It does not depend on claim 26. Therefore, the antibody disclosed by Sullivan et al. still meets the limitation of claim 28.

46. 4). Claim 26 is directed to a specific isolated antibody with deposit number. But it is not rejected.

47. Therefore, the antibody described by Sullivan et al. inherently meet the limitation of the claimed antibody. The rejection is therefore, maintained.

48.

49. Claims 23-24 and 28 are still rejected under 35 U.S.C. 102(b) as being anticipated by Thali et al. (J Virol. 1993 Jul; Vol. 6, No. 7, pp. 3978-88) or Kwong et al. (Nature 1998, Vol. *Nature* **393**, 648-659).

50. Thali et al. or Kwong et al. also teach two monoclonal antibodies, wherein one of them is 17b described above that can recognizes the conformational epitopes of HIV envelope protein gp 120 induced by soluble CD4 binding to said envelope protein and inhibit the HIV-1 infection (See entire document, especially, page 3980, Fig. 102 and Abstract for Thali et al. and page 654 for Kwong et al.). Therefore, the claims are still anticipated by the cited reference regardless the method for making the antibody may be different as discussed above.

51.

52. The rejection of claims 23-24 and 28 under 35 U.S.C. 102(b) as being anticipated by LaCasse et al. (Science 1999, Vol. 283, pp. 357-62) has been removed necessitated by

Applicants' amendment. Because LaCasse et al. only teach a whole serum, wherein the antibody is isolated. .

53. The rejection of claims 23-25 and 28 under 35 U.S.C. 102(b) as being anticipated by Gaudain et al. (Nature Medicine, 1997, Vol. 3, pp. 1389-1393) has been removed in view of Applicants' argument. Because the IgG1b 12 can recognize the overlapping site for CD4 binding to gp120, upon binding to the CD4 binding site, the gp120 does not form complex with CD4 as a complex.

54.

Claim Rejections - 35 USC § 102

55. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

56. Claims 23 and 28 are still rejected under 35 U.S.C. 102(a) as being anticipated by Dimitrov et al. (J. Human Virol. 2002, Vol. 5, No. 1 Abstract 118) on the same ground stated in the previous office action.

57. Applicants admit that Dimitrov describes using a phage display library to identify human monoclonal Fabs "which inhibited cell-cell fusion mediated by Envelope proteins of primary isolates from different clades". Dimitrov also describes a novel potent human monoclonal antibody Fab, X5, which binds with high affinity to gp 120 alone and higher affinity to its complex with CD4." However, Applicants still argue that Dimitrov et al. do not describe an antibody immunospecific for a fixed cell that includes an HIV envelope complex encoded by gp 160 and further wherein the envelope is complexed with a CD4 receptor. Dimitrov et al. also do not describe a hybridoma cell line under Deposit number PD03002, wherein the hybridoma produces DB-81. Since claims 24 and 28 depend from claims 23 and 26 respectively, claims 24 and 28 are not anticipated by Dimitrov et al. for at least the reasons described above. Applicant respectfully requests reconsideration and withdrawal of this rejection.

58. Applicants' argument has been fully considered; however, it is not found persuasive for the following reasons as discussed above:

59. 1). while the method of making an antibody taught by Dimitrov et al. is different from the one taught in the current Application; the claimed antibody has same structural and biological characteristics as claims drafted.

60. 2). While the claimed is now amended to an antibody immunospecific for cell comprising an HIV envelope complex encoded bybgp160 and further wherein the envelope binds to CD4, the envelope protein actually bound by the antibody could still be gp120 or usually is gp120. Because it is well known in the art that the gp160 is the precursor of HIV-1 envelope encoded by the full length of HIV-1 envelope glycoprotein gp160. when it is expressed as precursor protein, it is remained in the intracellular portion. Then it soon be cleaved into the membrane bound portion of envelope, i.e. gp120 and trans membrane domain of HIV-1 envelope of gp41. The method taught by specification **in example 2 on page 41** describe to immunize mice with cell expressing complex of gp120 and sCD4 on the cell surface. The gene used for transforming the cell can be either gene encoding the HIV-1 gp120 or the full length of HIV-1 envelope protein gene of gp160. However, upon the gene of gp160 is expressed in a eukaryotic cell, it is inherently cleaved into envelope protein gp120 and gp41 as the final product, unless the cell is deficient in such proteinase cleavage, wherein the CD4 binding site is located on the gp120. In the instant case, the specification does not teach that the cell can expressed uncleaved gp160 binding to CD4. It only teaches that the HIV-1 gp120 is expressed, which binds CD4 as a complex. The complex expressed by the cell is used as an antigen to induce the antibody. To this context, the antibody disclosed by Dimitrov et al. is same as the claimed antibody.

61. 3). The antibody cited in claim 28 is directed to a genus of antibodies that bind to the same idiotype of antibody produced by the hybridoma of claim 26. Therefore, it may include the antibody cited in claim 26, but it is not limited to the antibody of claim 26. Claim 28 is broader scope than claim 26. It does not depend on claim 26. Therefore, the antibody disclosed by Dimitrov et al. still meets the limitation of claim 28.

62. 4). Claim 26 is directed to a specific isolated antibody with deposit number. But it is not rejected.

63. Therefore, the antibody described by Dimitrov et al. inherently meet the limitation of the claimed antibody. The rejection is therefore, maintained.

Claim Rejections - 35 USC § 102/103

64. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

65. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

66. Claims 23-25 and 28 are still rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Dimitrov et al. (B) (US Patent No. 7,223,844B2) on the same ground stated in the previous office action.

67. In the response, Applicants admit that Dimitrov et al. in (B) describes an antibody induced by the "purified complexes of HIV envelope with CD4 and an HIV co-receptor, e.g., CCR5 or CXCR4, and active fragments thereof, which display broadly neutralizing activity against multiple genetic subtypes of HIV." Dimitrov et al. in (B) do not teach or suggest an isolated antibody immunospecific for a fixed cell that includes an HIV envelope complex encoded by gp 160 and further wherein the envelope is complexed with a CD4 receptor. Dimitrov et al in (B) also do not teach or suggest a hybridoma cell line under Deposit number PD03002, wherein the hybridoma produces DB-81. Since claims 24, 25 and 28 depend from claims 23 and 26 respectively, claims 24 and 28 are not patentable over Dimitrov et al. (B) for at least the reasons described above. Applicant respectfully requests reconsideration and withdrawal of this rejection.

68. Applicants' argument has been fully considered; however, it is not found persuasive for the following reasons as discussed above:

69. 1). While the method of making an antibody taught by Dimitrov et al. (B) is different from the one taught in the current Application; the antibody is same to the claimed antibody having same structural and biological characteristics as Applicants admitted above. Therefore, the claims are still anticipated by the cited reference.

70. 2). While the claimed is now amended to an antibody immunospecific for cell comprising an HIV envelope complex encoded bybgp160 and further wherein the envelope binds to CD4, the envelope protein actually bound by the antibody could still be gp120 or usually is gp120. Because it is well known in the art that the gp160 is the precursor of HIV-1 envelope encoded by the full length of HIV-1 envelope protein gp160. When it is first expressed as precursor, it is remained intra-cellular portion, then it is cleaved into the membrane bound portion of envelope, i.e. gp120 and trans membrane domain of HIV-1 envelope of gp41. The method taught by specification **in example 2 on page 41** describe to immunize mice with cell expressing complex of gp120 and sCD4 on the cell surface. The gene used for transforming the cell can be either gene encoding the HIV-1 gp120 or the full length of HIV-1 envelope protein gene of gp160. However, upon the gene of gp160 is expressed in a eukaryotic cell, it is inherently cleaved into envelope protein gp120 and gp41 as the final product, unless the cell is deficient in such proteinase cleavage, wherein the CD4 binding site is located on the gp120. In the instant case, the specification does not teach that the cell can expressed uncleaved gp160 binding to CD4. It only teaches that the HIV-1 gp120 is expressed, which binds CD4 as a complex. The complex expressed by the cell is used as an antigen to induce the antibody. To this context, the antibody disclosed by Dimitrov et al. is same as the claimed antibody.

71. 3). The antibody cited in claim 28 is directed to a genus of antibodies that bind to the same idiotype of antibody produced by the hybridoma of claim 26. Therefore, it may include the antibody cited in claim 26, but it is not limited to the antibody of claim 26. Claim 28 is broader scope than claim 26. It does not depend on claim 26. Therefore, the antibody disclosed by Dimitrov et al. (B) still meets the limitation of claim 28.

72. 4). Claim 26 is directed to a specific isolated antibody with deposit number. But it is not rejected.

73. Therefore, the antibody described by Dimitrov et al. (B) inherently meet the limitation of the claimed antibody. The rejection is therefore, maintained.

74. Or alternative, while Dimitrov et al. (B) do not show the data using said antibody fragment to treat HIV-1 infection, they suggests that said antibody fragment can be used for treatment of HIV infection (Column 12). Hence, the claimed invention as a whole is still considered prima facie obvious absence unexpected results. The rejection is maintained.

75. New ground rejections:

Claim Rejections - 35 USC § 112

76. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

77. Claims 23-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant case, the amendment of "an HIV envelope complex encoded by gp160" cited in claims 23-25 are not supported by the application as it was originally filed. Applicants do not have possession for having an isolated antibody binding to an HIV envelope complex encoded by gp160 as non-processed precursor protein.

Conclusion

Claim 26 is allowed.

78. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BAO LI whose telephone number is (571)272-0904. The examiner can normally be reached on 6:30 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Bao Qun Li/
Examiner, Art Unit 1648

/Bruce Campell/
Supervisory Patent Examiner, Art Unit 1648